REMARKS

Claims 47, 74, 101, 128, 155 and 182 are herein canceled without prejudice or disclaimer and Applicants reserve the right to pursue the subject matter of these claims in related applications. Claims 21, 48, 75, 102, 129 and 156 have been amended herein. Attached hereto is a marked-up version of the changes made by the current amendments, captioned "Version With Markings To Show Changes Made." The amendments are fully supported by the specification and claims as originally filed. Thus, no new matter has been added.

Claims 21-41, 43-46, 48-68, 70-73, 75-95, 97-100, 102-122, 124-127, 129-149, 151-154, 156-176 and 178-181 will be pending upon entry of these amendments. Applicants respectfully request reconsideration of the pending rejections in view of the amendments and remarks made herein.

I. Election/Restriction

In the instant Office Action (Paper No. 12), the Examiner acknowledges Applicants' election of Group I (in Paper No. 7), but contends that, "[b]ecause applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse." (Emphasis added).

Applicants respectfully disagree with the Examiner's allegation and assert that the response to the restriction requirement, as filed in Paper No. 7 on November 1, 2001, does indeed "distinctly and specifically point out the supposed errors in the restriction requirement." For example, the response lists the criteria for a proper restriction requirement and notes that the Examiner did not fulfill all of these criteria. Thus, Applicants identified an important error in the restriction requirement. Accordingly, Applicants respectfully request that the election be

treated as an election with traverse, and reserve the right to petition from the restriction requirement.

II. Objection to the Specification

The Examiner has objected to the specification as not fully compling with 37 C.F.R. §§ 1.821-1.825. Specifically, the Examiner points out that several sequences that appear in the specification are not listed in the sequence listing.

Applicants thank the Examiner for identifying this inadvertent clerical error and herein amend the sequence listing to list all sequences that appear in the specification and enter all appropriate SEQ ID numbers into the specification. Accordingly, Applicants submit that the Examiner's objection to the specification has been rendered moot.

III. Information Disclosure Statement

In the instant Office Action, the Examiner indicates that references AA and AB of the information disclosure statement filed November 1, 2001 have not been considered because copies of the documents were not provided.

Applicants respectfully disagree and submit herewith as evidence, a copy of the date-stamped postcard indicating in line item 4 that "copies of references AA-BW" were received by the Patent and Trademark Office on November 1, 2001 (*see* Exhibit A). However, for the Examiner's convenience, Applicants herewith provide duplicate copies of references AA and AB for the Examiner's consideration. In light of the evidence provided, Applicants respectfully submit that these references be accorded a submission date of November 1, 2001.

With regard to the Examiner's assertion that references AA and AB have also not been considered because they are "not published patent material," (Paper No. 12, page 3) Applicants

respectfully disagree and point out that 37 C.F.R. § 1.98(a) expressly provides for the listing of pending U.S. applications on information disclosure statements, regardless of their publication status. In particular, § 1.98(a)(1) lists "applications" as a separate category from patents and publications, and § 1.98(a)(2)(iii) specifically requires a legible copy of:

> each cited **pending U.S. application**, the application specification including the claims, and any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion. (Emphasis added). *See also* M.P.E.P. 609 at 600-120 to 121.

Thus, contrary to the Examiner's position, 37 C.F.R. § 1.98 clearly authorizes the citation of unpublished, pending U.S. patent applications in an information disclosure statement. Indeed, the Office's recent 21st Century Strategic Plan proposes to require applicants to disclose related applications.

Based on the above, U.S. Application Nos. 09/912,292 and 09/912,293 were properly submitted in the information disclosure statement filed November 1, 2001, and the Examiner has not provided a valid basis for failing to consider them. Accordingly, Applicants respectfully request that the Examiner consider references AA and AB and return the initialed form PTO/SB/08 (resubmitted herewith as Exhibit B) with the next office action, or provide Applicants with authority supporting her position.

IV. Rejections Under 35 U.S.C. § 112, first paragraph for deposit requirements

The Examiner has rejected claims 21, 26-41, 43-46, 48, 53-68, 70-73, 75, 80-95, 97-100, 102, 107-122, 124-127, 129, 134-149, 150-154, 156, 161-176 and 178-181 under 35 U.S.C. § 112, first paragraph, for alleged lack of enablement. Specifically, the Examiner contends

> It is noted that applicants have deposited the organisms but there is no indication in the specification as to public availability. As the deposited has been made under the terms of the Budapest Treat (p 9, lines 14-17), then an affidavit or declaration by applicants, or a statement by an attorney of record

> over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein.

See Paper No. 12, pages 3-4.

In compliance with the Examiner's request, Applicants submit herewith as Exhibit C a Statement Concerning the Deposited cDNA Clone, signed by the attorney of record, which states that the strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon issuance of a patent. In light of the Statement, Applicants respectfully request that the rejection be reconsidered and withdrawn.

V. Rejections Under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 21, 30-41, 43-46, 48-68, 70-73, 75-95, 97-100, 102, 111-122, 124-127, 129-149, 151-154, 156-176 and 178-181 under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Specifically, the Examiner contends

> ... [The specification] does not show what features are unique to identity of a molecular variant as encoding ICE-LAP-3 or 4. There is no predictability as to which residues may be substituted so that the molecule to [sic] can be identified as encoding either ICE-LAP 3 or 4, i.e., what distinguishes these from other members of the gene family. How is one to determine whether a given gene with 95% identity e.g., is a derivative of either ICE-LAP 3 or 4 or another member of the ICE family?
>
> With respect to fragments of the genes, the specification provides no guidance regarding which fragments are useful for any purpose. While one can randomly make fragments, there is no predictability as to how they may be used.

See Paper No. 12, pages 5-6.

Applicants respectfully disagree and traverse.

Preliminarily, Applicants point out that claims 48, 75, 129 and 156 have been amended herein to recite "wherein said polynucleotide encodes a polypeptide having ICE-LAP 3 [or 4] activity." In light of this amendment, claims 48, 75, 129 and 156, and claims 49-68, 70-73, 74-95, 97-100, 102, 111-122, 124-127, 130-149, 151-154, 157-176 and 178-181, which depend therefrom, clearly encompass polynucleotides encoding polypeptides that are derivatives of either ICE-LAP 3 or 4. Accordingly, the Examiner's rejection is moot with respect to these claims.

With regard to claims 21, 30-41, 43-46, 102, 111-122 and 124-127, Applicants respectfully assert that they are fully enabled. Firstly, Applicants point out that in order to enable the claimed invention as required by 35 U.S.C. § 112, first paragraph, the specification need only enable a person of ordinary skill in the art to make the claimed nucleic acids and practice a single use of the claimed nucleic acids without undue experimentation. See *Raytheon Co. v. Roper Corp.*, 220 U.S.P.Q. 592 (Fed. Cir. 1983, *cert. denied*, 469 U.S. 835 (1984); *Ex parte Lanham*, 121 U.S.P.Q. 223 (Pat. Off. Bd. App. 1958). Applicants submit that the claimed nucleic acids are enabled, such as, for example, for use as a probe, or to encode a polypeptide that binds an antibody to an ICE-LAP 3 or 4 polypeptide. For example, nucleic acids of the invention, such as nucleic acids encoding polypeptides of the invention, would be useful, for example, as probes, and/or to routinely generate antibodies that specifically bind ICE-LAP 3 or 4. The specification teaches that antibodies generated against ICE-LAP 3 or 4 polypeptides of the invention and other compositions of the invention may be used in, for example, protein purification and in diagnostic and therapeutic techniques, including, but not limited to, treating diseases and disorders associated with non-programmed necrotic cell death (e.g., Alzheimer's disease, Parkinson's disease and rheumatoid arthritis) (See for example, the Specification at page 18, lines 23-28; and page 19, lines 23-29).

Furthermore, "[t]here is no magical relation between the number of representative examples and the breadth of the claims" with respect to enablement. *In re Borkowski*, 164 U.S.P.Q. 642, 646 (C.C.P.A. 1970). The issue is not whether the specification discloses any or all alterations that can be made in the claimed nucleic acids (or polypeptides encoded by the claimed nucleic acids) that will not alter the functional activity of the nucleic acids or polypeptides encoded thereby, but rather whether nucleic acids encompassed by the claims have at least a single use, and whether this use can be confirmed, without undue experimentation, by following procedures either described in the specification or otherwise known in the art. See *In re Angstadt*, 190 U.S.P.Q. 214, 218 (C.C.P.A. 1976):

> To require such a complete disclosure would apparently necessitate a patent with "thousands of examples . . . More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments . . .

While the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of the experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue:

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

In re Angstadt, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976) (emphasis in the original).

As Judge Rich explained in *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1445 (Fed. Cir. 1991), the statutory enablement requirement is satisfied if the specification "adequately guides the worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility." (Emphasis provided). Since the disclosed or otherwise known methods of making and screening nucleic acids (including fragments) and polypeptides encoded thereby may be used to make and then determine, without undue experimentation, whether a given nucleic acid encompassed by the claims is able to function as a probe or to encode a polypeptide that binds an antibody to ICE-LAP 3 or 4, the enablement requirement is fully satisfied. *In re Wands*, 8 U.S.P.Q.2d at 1404; *Ex parte Mark*, 12 U.S.P.Q.2d 1904, 1906-1907 (B.P.A.I. 1989). Accordingly, the Examiner's insistence that the specification must identify "[w]hich are specific ICE-LAP 3 and/or 4 probes" and "which ones should be chosen [for raising antisera]" (Paper No. 12, page 5, first paragraph) is inconsistent with the law.

In view of the above discussion, Applicants believe the Examiner's concerns have been fully addressed. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 21, 30-41, 43-46, 48-68, 70-73, 75-95, 97-100, 102, 111-122, 124-127, 129-149, 151-154, 156-176 and 178-181.

VI. Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claims 21, 28, 32-41, 43-46, 48, 55, 59-68, 70-73, 75, 82, 86-95, 97-100, 102, 109, 113-122, 124-127, 129, 136, 140-149, 151-154, 156, 163, 167-176 and 177-181 under 35 U.S.C. § 112, second paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. *See* Paper No. 12, page 5. In particular, the Examiner has rejected part (g) of claims

21, 48, 75, 102, 129 and 156 and claims dependent thereon, stating "[i]t is unclear what is meant by this term [mature portion of the polypeptide] – is a fragment of the mature polypeptide intended, or the portion of the encoded polypeptide that becomes the mature protein?" *Id.*

Applicants respectfully disagree and traverse, and assert that one of skill in the art would know what is intended by the phrase "mature portion of the polypeptide." However, solely in the interest of facilitating prosecution, Applicants have amended subpart (g) of claims 21, 48, 75, 102, 129 and 156 to recite "a polynucleotide encoding the mature polypeptide encoded by the human cDNA in ATCC Deposit No: 75875." Applicants note that this amendment does not in any way alter the meaning or scope of the claims.

In light of the amendments made herein, Applicants assert that the claims as amended particularly point out and distinctly claims the subject matter which applicant regards as the invention. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 21, 28, 32-41, 43-46, 48, 55, 59-68, 70-73, 75, 82, 86-95, 97-100, 102, 109, 113-122, 124-127, 129, 136, 140-149, 151-154, 156, 163, 167-176 and 177-181 under 35 U.S.C. § 112, second paragraph.

VII. Provisional Obviousness-Type Double Patenting Rejection

The Examiner has rejected claims 21-41, 43-46, 48-68, 70-73, 75-95, 97-100, 102-122, 124-126, 128-149, 151-154, 156-176 and 178-181 as being provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 43, 44 and 46 of copending Application No. 08/334, 251.

In accordance with the guidelines (*see*, for example, M.P.E.P. § 804), Applicants respectfully refrain from taking action until at least one of the pending applications has allowable claims.

Conclusion

Applicants respectfully request that the above-made amendments and remarks be entered and made of record in the file history of the instant application. Applicants believe that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite prosecution, the undersigned can be reached at the telephone number indicated below.

If there are any fees due in connection with the filing of this paper, please charge the fees to Deposit Account No. 08-3425.

Dated: November 13, 2002

Respectfully submitted,

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VIA HAND DELIVERY NOVEMBER 13, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
He et al.

Docket No.: PF140P1D1

Application No.: 09/613,508

Group Art Unit: 1653

Filed: July 10, 2000

Examiner: G. Bugaisky

For: Interleukin-1 β Converting Enzyme Like Apoptosis Protease-3 and 4

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The first paragraph on page 1 has been amended as follows.

This application is a divisional of Application No. 08/462,969, filed June 5, 1995, now U.S. Patent No. 6,087,150, granted July 11, 2000, which is a continuation-in-part of Application Serial No. 08/334,251, filed November 1, 1994, each of which is hereby incorporated by reference in its entirety.

The paragraph beginning on page 1, line 21, through page 2, line 14, has been amended as follows.

In the nematode *caenorhabditis elegans*, a genetic pathway of programmed cell death has been identified (Ellis, R.E., et al. Annu. Rev. Cell Biol., 7:663-698 (1991)). Two genes, *ced-3* and *ced-4*, are essential for cells to undergo programmed cell death in *C. elegans* (Ellis, H.M., and Horvitz, H.R., Cell, 44:817-829 (1986)). Recessive mutations that eliminate the function of these two genes prevent normal programmed cell death during the development of *C. elegans*. The known vertebrate counterpart to *ced-3* protein is ICE. The overall amino acid identity between *ced-3* and ICE is 28%, with a region of 115 amino acids (residues 246-360 of

3 (SEQ ID NO:13) and 164-278 of ICE (SEQ ID NO:14)) that shows the highest identity (43%). This region contains a conserved pentapeptide, QACRG (residues 356-360 of *ced-3* (SEQ ID NO:13)), which contains a cysteine known to be essential for ICE function. The ICE-LAP-1 and 2 polypeptides of the present invention also have the same conserved pentapeptide and the cysteine residue which is essential for ICE function.

The last paragraph on page 4 has been amended as follows.

Figures 3A-B shows an amino acid sequence comparison between ICE-LAP-3 (SEQ ID NO:2), ICE-LAP-4 (SEQ ID NO:4), human ICE (SEQ ID NO:14) and the C. elegans cell death gene ced-3 (SEQ ID NO:13). Shaded areas represent amino acid matches between the different sequences.

The paragraph on page 5, lines 11-24, has been amended as follows.

The polynucleotide encoding ICE-LAP-3 can be detected from human prostate, human endometrial tumor, human pancreatic tumor, human adrenal gland tumor and human tonsil. The full-length encoding ICE-LAP-3 was discovered in a cDNA library derived from human endometrial tumor. It is structurally related to the Interleukin-1 converting enzyme family. It contains an open reading frame encoding a protein of approximately 341 amino acid residues. The protein exhibits the highest degree of homology to *C. elegans* cell death gene ced-3 which is a homolog of human interleukin-1 converting enzyme, with 68 % similarity and 43 % identity over the entire amino acid sequence. It should be pointed out that the pentapeptide QACRG is conserved and is located at amino acid position 184-188 of the sequence shown in SEQ ID NO:2.

The paragraph on page 5, lines 25-33, has been amended as follows.

The polynucleotide encoding ICE-LAP-4 was discovered in a cDNA library derived from human tonsils. It is structurally related to the ICE family. It contains an open reading frame encoding a protein of about 277 amino acid residues. The protein exhibits the highest degree of homology to the *C. elegans* cell death gene ced-3 with 29 % identity and 46 % similarity over a 277 amino acid stretch. It is also important that the pentapeptide QACRG is conserved and is located at amino position 161-165 of the sequence shown in SEQ ID NO:4.

In the claims:

Claims 47, 74, 101, 128, 155 and 182 have been canceled herein, and claims 21, 48, 75, 102, 129 and 156 have been amended as follows.

21. (Once Amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;

(b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and

(k) a polynucleotide having a sequence complementary to the polynucleotide sequence of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j).

48. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 90% or more identical to a second polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;

(b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and

(k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 4 activity.

75. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 95% or more identical to a second polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 303 of SEQ ID NO:2;

(b) a polynucleotide encoding amino acid residues 2 to 303 of SEQ ID NO:2;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:2;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:2;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75875;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75875, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75875; and

(k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 4 activity.

102. (Once Amended) An isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;

(b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and

(k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j).

129. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 90% or more identical to a second polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;

(b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and

(k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 3 activity.

156. (Once Amended) An isolated nucleic acid molecule comprising a first polynucleotide 95% or more identical to a second polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acid residues 1 to 277 of SEQ ID NO:4;

(b) a polynucleotide encoding amino acid residues 2 to 277 of SEQ ID NO:4;

(c) a polynucleotide encoding at least 30 contiguous amino acid residues of SEQ ID NO:4;

(d) a polynucleotide encoding at least 50 contiguous amino acid residues of SEQ ID NO:4;

(e) a polynucleotide encoding the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(f) a polynucleotide encoding the polypeptide minus the N-terminal methionine encoded by the human cDNA in ATCC Deposit No: 75873;

(g) a polynucleotide encoding ~~a~~ the mature ~~portion of the~~ polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(h) a polynucleotide encoding a fragment of a polypeptide encoded by the human cDNA in ATCC Deposit No: 75873, wherein said fragment has enzymatic activity;

(i) a polynucleotide encoding at least 30 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873;

(j) a polynucleotide encoding at least 50 contiguous amino acid residues of the polypeptide encoded by the human cDNA in ATCC Deposit No: 75873; and

(k) a polynucleotide having a sequence complementary to the polynucleotide of (a), (b), (c), (d), (e), (f), (g), (h), (i), or (j),

wherein said polynucleotide encodes a polypeptide having ICE-LAP 3 activity.

Exhibit C

```
LOCUS       HSU39613      912 bp    mRNA            PRI       19-JAN-1996
DEFINITION  Human cysteine protease ICE-LAP3 mRNA, complete cds.
ACCESSION   U39613
NID         g1125072
KEYWORDS    .
SOURCE      human.
  ORGANISM  Homo sapiens
            Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
            Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 912)
  AUTHORS   Duan,H., Chinnaiyan,A.M., Hudson,P.L., Wing,J.P., He,W.W. and
            Dixit,V.M.
  TITLE     ICE-LAP3, a novel mammalian homologue of the Caenorhabditis elegans
            cell death protein Ced-3 is activated during Fas- and tumor
            necrosis factor-induced apoptosis
  JOURNAL   J. Biol. Chem. 271 (3), 1621-1625 (1996)
  MEDLINE   96139498
REFERENCE   2  (bases 1 to 912)
  AUTHORS   Duan,H., Chinnaiyan,A.M., Hudson,P.L., Wing,J.P., He,W.W. and
            Dixit,V.M.
  TITLE     Direct Submission
  JOURNAL   Submitted (27-OCT-1995) Hangjun Duan, Pathology, University of
            Michigan, 1150 W Medical Center Dr MSRBI Room 7514, Ann Arbor, MI
            48109, USA
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                     DLTAHFRGDRCKTLLEKPKLFFIQACRGTELDDAIQADSGPINDTDANPRYKIPVEAD
                     FLFAYSTVPGYYSWRSPGRGSWFVQALCSILEEHGKDLEIMQILTRVNDRVARHFESQ
                     SDDPHFHEKKQIPCVVSMLTKELYFSQ"
BASE COUNT      263 a    219 c    223 g    207 t
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      901 ttcagtcaat ag
//
```